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EXAMINER

RAO, MANJUNATH N

|          |              |
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| ART UNIT | PAPER NUMBER |
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1652

DATE MAILED: 01/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/576,778

Applicant(s)

SCHULEIN ET AL.

Examiner

Manjunath N. Rao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 10 October 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 62-81 is/are pending in the application.
- 4a) Of the above claim(s) 80 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 62-67, 72-79 and 81 is/are rejected.
- 7) ☒ Claim(s) 68-71 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

Claims 62-81 are currently pending and are present for examination. Claims 62-79 and 81 are now under consideration. Claim 80 remains withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. However, when claims 62-79, 81 directed to a product, become allowable, pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86), claim 80, directed to the process of using the patentable product, will be rejoined by the Examiner.

Applicants' amendments and arguments filed on 10-10-03, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 72-73 and claim 74 which depends from claim 73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 72-73 recite the phrase "one or more of nucleotides 76-1455 of SEQ ID NO:1". It is not clear to the Examiner as to what applicants mean by the above phrase. It appears that applicants are intending to claim a polypeptide encoded by a polynucleotide that hybridizes to "nucleotides 76-

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1455 of SEQ ID NO:1". If this is so amending the claim accordingly by deleting the phrase "one or more" would overcome this rejection.

Claims 75-79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 75-79 depend from cancelled claims and are therefore rendered indefinite. Correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 62-67, 72-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an  $\beta$  1,4-endoglucanase enzyme with SEQ ID NO:2 or amino acids 1-456 or 1-617 of SEQ ID NO:2 with an optimum temperature of 65° C when measured at a pH of 7.5, active at a pH in the range of 4-11, and isolated from *B.licheniformis*, does not reasonably provide enablement for any such enzyme that has 85%, 90%, 95% or 98% sequence identity with amino acids 1-456 or 1-617 of SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1)

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the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 62-67, 72-74 are so broad as to encompass any  $\beta$  1,4-endoglucanase enzyme that has 85%, 90%, 95% or 98% sequence identity with amino acids 1-456 or 1-617 of SEQ ID NO:2. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of  $\beta$  1,4-endoglucanases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single  $\beta$  1,4-endoglucanase.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

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The specification does not support the broad scope of the claims which encompass all modifications and fragments of any  $\beta$  1,4-endoglucanase having 85% through 98% identity to SEQ ID NO:2 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting endoglucanase activity; (B) the general tolerance of  $\beta$  1,4-endoglucanase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any  $\beta$  1,4-endoglucanase amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including  $\beta$  1,4-endoglucanases with an enormous number of amino acid modifications of the  $\beta$  1,4-endoglucanase SEQ ID NOS: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of  $\beta$  1,4-endoglucanases having the desired characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants have traversed the above rejection and argue that the rejection under 35 U.S.C. §112, first paragraph is not proper because the specification contains an extensive disclosure of how one skilled in the art can make and use the polypeptides of the present invention. For example, applicants point out that the specification teaches hybridization techniques as well as mutagenesis techniques. Applicants also argue that those

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skilled in the art would know where to obtain the strains that produce the above enzyme and methods to screen the strains are taught in the art and the specification. Examiner respectfully disagrees with such an argument being persuasive to overcome the above rejection. This is because, because while methods to screen and isolate source microorganism for the above enzyme and methods to produce variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan, producing variants as claimed by applicants (i.e., amino acid sequences having endoglucanase activity and that are 85% through 98% identical to SEQ ID NO:2) requires that one of ordinary skill in the art know or be provided with guidance as which specific amino acids in SEQ ID NO:L2 can be changed or altered as well as guidance for the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities (i.e., replacing every one of the 617 amino acids with any one of the twenty other amino acids followed by testing each and every sequence for the activity). This would clearly constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting endoglucanase activity; (B) the general tolerance of  $\beta$  1,4-endoglucanase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any  $\beta$  1,4-endoglucanase amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides

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insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Therefore the above rejection is maintained.

Examiner has withdrawn the previous rejection of claims rejected under 35 U.S.C. 102(b) as being anticipated by Dhillon et al. (Biotechnol. Lett, Vol. 7(9):695-697, 1985). In view of the applicants response and amendment. Applicants have clearly pointed out that the optimum temperature of the reference enzyme is 55 °C as opposed to the claimed optimum temperature of 65 °C thereby showing that the two enzymes are different.

Examiner has also withdrawn the rejection of claim 59 under 35 U.S.C. 103(a) as being unpatentable over Dhillon et al. as applied to claims 43-58, 60-61, and further in view of Olsen et al. (WO 95/26398, 10-5-1995) as applicants have overcome the effects of Dhillon et al. reference.

### ***Conclusion***

Claims 68-71 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).



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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 7:30 a.m. to 4:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

  
MANJUNATH RAO  
PATENT EXAMINER

Manjunath N. Rao Ph.D.

1/5/04